

IN THE CLAIMS:

Please amend the claims as follows:

Claims 1-7 - CANCELED

8. (Currently Amended) A pharmaceutical preparation, comprising,
a therapeutically effective amount of at least one compound of the formula I as
claimed in at least one of claims ~~1 to 6~~ and/or 14 to 19 or its physiologically tolerable
salts, and
a pharmaceutically acceptable carrier.
9. (Currently Amended) A pharmaceutical composition comprising,
a therapeutically effective amount of a compound of the formula I as claimed in at
least one of claims ~~1 to 6~~ and/or 14 to 19 and their physiologically tolerable salts, or
~~and/or~~ their prodrugs for inhibition of factor Xa and/or factor VIIa or for influencing blood
coagulation or fibrinolysis.
10. (Currently Amended) A method of treating blood coagulation disorders,
~~inflammatory response, inflammation,~~ fibrinolysis, cardiovascular disorders,
~~thromboembolic diseases, restenoses, restenosis, abnormal thrombus formation, acute-~~
~~myocardial infarction, unstable angina, acute vessel closure associated with-~~
~~thrombolytic therapy, thromboembolism, percutaneous, pathologic thrombus formation-~~
~~occurring in the veins of the lower extremities following abdominal, knee and hip surgery,~~
~~transluminal coronary angioplasty, transient ischemic attacks, stroke a risk of pulmonary~~
~~thromboembolism, certain viral infections or cancer, intravascular coagulopathy-~~
~~occurring in vascular systems during septic shock, coronary heart disease, myocardial-~~

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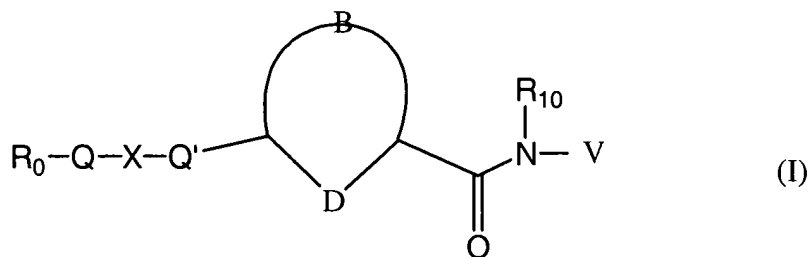
~~infarction, angina pectoris, vascular restenosis, for example restenosis following angioplasty like PTCA, adult respiratory distress syndrome, multi-organ failure, stroke and disseminated intravascular clotting disorder, and thrombosis thromboses like deep vein and proximal vein thrombosis which can occur following surgery comprising administration of administering the pharmaceutical composition preparation of claim 8 9 to a host in need thereof.~~

11. (Currently Amended) A prodrug of the compound of the formula I as claimed in ~~at least one of claims 1 to 6~~ claim 9, wherein the prodrug is chosen from an acyl prodrug, a carbamate prodrug, an ester prodrug, and an amide prodrug.

12. (Previously Presented) The (C₁-C₆)-acyl prodrug according to claim 11.

13. (Previously Presented) The (C₁-C₆)-alkyloxycarbonyl prodrug according to claim 11.

14. (New) A compound of formula (I),



wherein;

R₀ is phenyl, wherein phenyl is mono-, di- or

trisubstituted independently of one another by R², or a mono- or bicyclic 5- to 10-membered heteroaryl containing one or two nitrogen atoms as ring heteroatoms, wherein heteroaryl is unsubstituted or mono-, di- or trisubstituted independently of one another by R² ;

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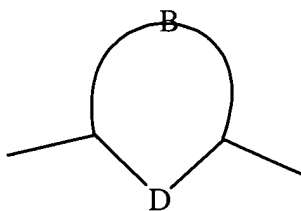
R^2 is $-\text{NO}_2$; halogen; $-\text{CN}$; $-\text{OH}$; $-\text{NH}_2$; $(\text{C}_1\text{-C}_8)\text{-alkyloxy-}$, wherein alkyloxy is unsubstituted or mono-, di- or trisubstituted independently of one another by halogen, amino group, hydroxy group or methoxy group; or $-(\text{C}_1\text{-C}_8)\text{-alkyl}$, wherein alkyl is unsubstituted or mono-, di- or trisubstituted independently of one another by halogen, amino group, hydroxy group or methoxy group;

Q and Q' are different and are a direct bond, or $-\text{O}-$;

R_{10} is a hydrogen atom, or $(\text{C}_1\text{-C}_4)\text{-alkyl-}$;

X is $(\text{C}_1\text{-C}_6)\text{-alkylene}$, wherein alkylene is unsubstituted or mono-, di- or trisubstituted independently of one another by halogen, amino group or a hydroxy group;

the substructure of formula III



(III)

wherein B, together with D and the two carbon atoms to which D is attached, represents

a) a mono- or bicyclic 5- to 10-membered carbocyclic aryl group, wherein said 5- to 10-membered carbocyclic aryl group is unsubstituted or mono-, di- or trisubstituted independently of one another by R^1 ;


b) phenyl, wherein phenyl is unsubstituted or mono-, di- or trisubstituted independently of one another by R^1 ;

c) a mono- or bicyclic 5-to 10-membered heterocyclic group (Het), containing one or more heteroatoms chosen from nitrogen, sulfur, and oxygen, wherein

said Het group is unsubstituted or mono-, di- or trisubstituted independently of one another by R^1 ; or

d) pyridyl, wherein pyridyl is unsubstituted or mono-, di- or trisubstituted independently of one another by R^1 ;

D is carbon, oxygen, sulfur, or nitrogen;



R^1 is a halogen; -OH; -SO₂-NH₂; -NO₂; -CN; $R^{11}R^{12}N$ -, wherein $R^{11}R^{12}$ independently of one another are a hydrogen atom, (C₁-C₄)-alkyl-, or (C₁-C₆)-acyl-; (C₁-C₈)-alkylamino-, (C₁-C₈)-alkyloxy-, (C₁-C₈)-alkyl-, hydroxycarbonyl-(C₁-C₈)-alkylureido-, (C₁-C₈)-alkyloxycarbonyl-(C₁-C₈)-alkylureido-, or (C₁-C₈)-alkylsulfonyl-, wherein the alkyl of each group is unsubstituted or mono-, di- or trisubstituted independently of one another by R^{13} ; (C₆-C₁₄)-aryl, wherein aryl is unsubstituted or mono-, di- or trisubstituted independently of one another by R^{13} ; or -C(O)-NR¹⁴R¹⁵, wherein $R^{14}R^{15}$ independently of one another are hydrogen atom or (C₁-C₄)-alkyl-, or

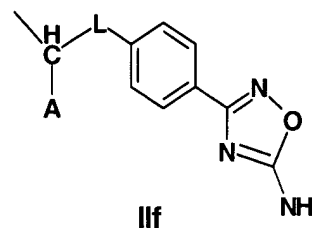
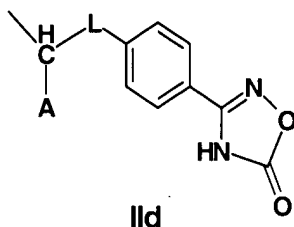
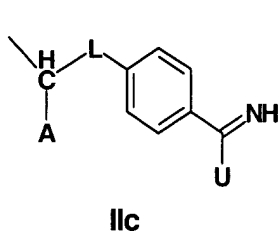
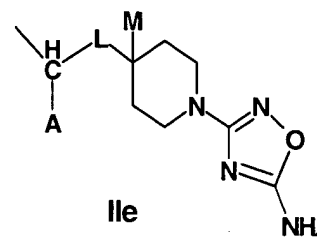
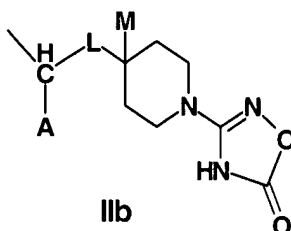
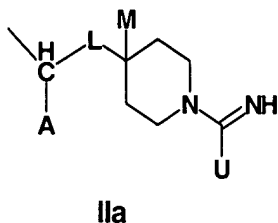
two R^1 residues bonded to adjacent ring carbon atoms together with the carbon atoms to which they are bonded form an aromatic ring condensed to the ring depicted in formula I, where the ring formed by the two R^1 residues is unsubstituted or mono-, di- or trisubstituted independently of one another by R^{13} , R^{11} and R^{12} together with the nitrogen atom to which they are bonded form a saturated or unsaturated 5- to 6-membered monocyclic heterocyclic ring which in addition to the nitrogen atom carrying R^{11} and R^{12} can contain one or two identical or different ring heteroatoms chosen from oxygen, sulfur and nitrogen, and in which one or two of the ring carbon atoms can be substituted by oxo to form C(O)- residue(s);

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R^{13} is halogen, $-\text{NO}_2$, $-\text{CN}$, $-\text{OH}$, $(\text{C}_1\text{-C}_8)\text{-alkyl-}$, $(\text{C}_1\text{-C}_8)\text{-alkyloxy-}$, $-\text{CF}_3$, or $-\text{NH}_2$;
and

V is a residue of the formulae IIa, IIb, IIc, IId, IIe or IIf;



wherein

L is a direct bond or $(\text{C}_1\text{-C}_3)\text{-alkylene}$, wherein the alkylene is unsubstituted or mono-, di- or trisubstituted independently of one another by A;

A is a hydrogen atom; $-\text{C}(\text{O})\text{-OH}$; $-\text{C}(\text{O})\text{-O-}(\text{C}_1\text{-C}_4)\text{-alkyl}$, or $(\text{C}_1\text{-C}_4)\text{-alkyl-}$, wherein the alkyl of each group is unsubstituted or mono-, di- or tri- substituted independently of one another by $-\text{OH}$, $-\text{NH}_2$ or $-(\text{C}_1\text{-C}_4)\text{-alkoxy}$; $-\text{C}(\text{O})\text{-NR}^4\text{R}^5$; $-\text{SO}_2\text{-NH}_2$; or $-\text{SO}_2\text{-CH}_3$;

U is $-\text{NH}_2$, $(\text{C}_1\text{-C}_4)\text{-alkyl-}$, $-\text{NH-C}(\text{O})\text{-O-}(\text{C}_1\text{-C}_4)\text{-alkyl}$, or $-\text{NH-C}(\text{O})\text{-O-}(\text{C}_1\text{-C}_4)\text{-alkyl-aryl}$;

M is a hydrogen atom, $(\text{C}_1\text{-C}_3)\text{-alkyl-}$, or $-\text{OH}$,

R^4 and R^5 are independently of one another identical or different and are a hydrogen atom; $(\text{C}_1\text{-C}_{12})\text{-alkyl-}$, wherein alkyl is unsubstituted or mono-, di- or

trisubstituted independently of one another by R^{13} as defined above; (C_6-C_{14}) -aryl- (C_1-C_4) -alkyl-, wherein alkyl and aryl are unsubstituted or mono-, di- or trisubstituted independently of one another by R^{13} as defined above; (C_6-C_{14}) -aryl-, wherein aryl is unsubstituted or mono-, di- or trisubstituted independently of one another by R^{13} as defined above; Het-, wherein Het- is unsubstituted or mono-, di- or trisubstituted independently of one another by R^{13} as defined above; or Het- (C_1-C_4) -alkyl-, wherein alkyl and Het- are unsubstituted or mono-, di- or trisubstituted independently of one another by R^{13} as defined above; or

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R⁴ and R⁵ together with the nitrogen atom to which they are bonded form a saturated 3- to 8-membered monocyclic heterocyclic ring which in addition to the nitrogen atom carrying R⁴ and R⁵ can contain one or two identical or different ring heteroatoms chosen from oxygen, sulfur and nitrogen;

in all its stereoisomeric forms and mixtures thereof in any ratio, or its physiologically tolerable salts.

15. (New) A compound of formula I as claimed in claim 14, wherein

R₀ is phenyl, wherein phenyl is mono-, di- or trisubstituted independently of one another by R²; or pyridyl, wherein pyridyl is unsubstituted or mono-, di- or trisubstituted independently of one another by R²;

R² is -NO₂; halogen; -CN; -OH; -NH₂; (C_1-C_4) -alkyloxy-, wherein alkyloxy is unsubstituted or mono-, di- or trisubstituted independently of one another by halogen, amino group, hydroxy group or methoxy group; or (C_1-C_4) -alkyl, wherein alkyl is unsubstituted or mono-, di- or trisubstituted independently of one another by halogen, amino group, hydroxy group or methoxy group;

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Q, Q', X, R¹, R¹¹ and R¹² are as defined in claim 14,

D is carbon or nitrogen,

the substructure of formula III is phenyl or pyridyl, wherein phenyl and pyridyl independently of one another are unsubstituted or mono-, di- or trisubstituted independently of one another by R¹;

R¹³ is halogen, -NO₂, -CN, -OH, (C₁-C₄)-alkyl-, (C₁-C₄)-alkyloxy-, -CF₃, or -NH₂;

R₁₀ is a hydrogen atom or methyl; and

V is a fragment of formulae IIa, IIb, IIc, IId, IIe, or II f as defined above; wherein

L, U, M, R⁴ and R⁵ are as defined in claim 14, and

A is hydrogen atom; -C(O)-OH; -C(O)-O-(C₁-C₄)-alkyl, or (C₁-C₄)-alkyl-, wherein the alkyl of each group is unsubstituted or mono-, di- or tri- substituted independently of one another by -OH, -NH₂ or -(C₁-C₄)-alkoxy; or -C(O)-NR⁴R⁵.

16. (New) A compound of the formula I as claimed in claim 14, wherein

R₀ is phenyl or pyridyl, wherein phenyl and pyridyl independently of one another are mono-, di- or trisubstituted independently of one another by R²;

R² is -NH₂; halogen; -CN; -OH; (C₁-C₄)-alkyloxy-, wherein alkyloxy is unsubstituted or substituted by an amino group; or -(C₁-C₄)-alkyl, wherein alkyl is unsubstituted or substituted by an amino group;

Q and Q' are different and are a direct bond or -O-;

X is a (C₁-C₄)-alkylene, wherein alkylene is unsubstituted or mono-, di- or tri-substituted independently of one another by halogen, amino group or a hydroxy group;

D is carbon or nitrogen;

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the substructure of formula III is phenyl or pyridyl, wherein phenyl and pyridyl independently of one another are unsubstituted or mono-, di- or trisubstituted independently of one another by R¹;

R¹ is halogen; -OH; -SO₂-NH₂; -NO₂; -CN; -NH₂; (C₁-C₄)-alkylamino-, (C₁-C₄)-alkyloxy-, (C₁-C₄)-alkyl-, or (C₁-C₄)-alkylsulfonyl-, wherein the alkyl of each group is unsubstituted or mono-, di- or trisubstituted independently of one another by R¹³; (C₆-C₁₄)-aryl, wherein aryl is unsubstituted or mono-, di- or trisubstituted independently of one another by R¹³; -C(O)-NR¹⁴R¹⁵, wherein R¹⁴R¹⁵ independently of one another are hydrogen atom or (C₁-C₄)-alkyl-; R¹¹R¹²N-, wherein R¹¹ and R¹² are as defined above; or -NR⁴R⁵;

R¹³ is halogen, -NO₂, -CN, -OH, (C₁-C₄)-alkyl-, (C₁-C₄)-alkyloxy-, -CF₃, or -NH₂;

R₁₀ is a hydrogen atom or methyl; and

V is a fragment of formulae IIa, IIb, IIc, IId, IIe or II f as defined above, wherein

L is a direct bond or (C₁-C₃)-alkylene-;

A is a hydrogen atom, -C(O)-OH, -C(O)-O-(C₁-C₄)-alkyl, -C(O)-NR⁴R⁵, or (C₁-C₄)-alkyl-;

U is -NH₂, methyl, -NH-C(O)-O-(C₁-C₄)-alkyl, or -NH-C(O)-O-(CH₂)-phenyl;

M is a hydrogen atom, (C₁-C₃)-alkyl-, or -O; and

R⁴ and R⁵ are independently of one another a hydrogen atom or (C₁-C₄)-alkyl-.

17. (New) A compound of formula I as claimed in claim 14, wherein

R₀ is phenyl or pyridyl, wherein phenyl and pyridyl independently of one another are mono-, di- or trisubstituted independently of one another by R²;

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R² is a halogen; -CN; (C₁-C₄)-alkyloxy-, wherein alkyloxy is unsubstituted or substituted by halogen or an amino group; or -(C₁-C₄)-alkyl, wherein alkyl is unsubstituted or substituted by an amino group or halogen;

Q and Q' are different and are a direct bond, or -O-;

X is -(C₁-C₃)-alkylene-, wherein alkylene is unsubstituted or mono-, di- or trisubstituted independently of one another by halogen, amino group or hydroxy group;

D is carbon;

the substructure of formula III is phenyl, wherein phenyl is unsubstituted or mono-, di- or trisubstituted independently of one another by R¹;

R¹ is halogen; -NO₂; -CN; -NH₂; -OH; -SO₂-NH₂; (C₁-C₄)-alkylamino-, (C₁-C₄)-alkyloxy-, (C₁-C₄)-alkyl-, or (C₁-C₄)-alkylsulfonyl-, wherein the alkyl of each group is unsubstituted or mono-, di- or trisubstituted independently of one another by R¹³; (C₆-C₁₄)-aryl, wherein aryl is unsubstituted or mono-, di- or trisubstituted independently of one another by R¹³; -C(O)-NR¹⁴R¹⁵, wherein R¹⁴R¹⁵ independently of one another are hydrogen atom or (C₁-C₄)-alkyl-; R¹¹R¹²N-, wherein R¹¹ and R¹² are as defined above; or -NR⁴R⁵;

R¹³ is halogen, -CF₃, -NH₂, -OH, (C₁-C₄)-alkyl-, or (C₁-C₄)-alkyloxy-;

R₁₀ is a hydrogen atom; and

V is a fragment of the formulae IIa, IIb, IIc or IId as defined above, wherein

L is a direct bond or (C₁-C₂)-alkylene-;

A is a hydrogen atom, -C(O)-OH, -C(O)-O-(C₁-C₄)-alkyl, -C(O)-NR⁴R⁵, or (C₁-C₄)-alkyl;

U is -NH₂, methyl, -NH-C(O)-O-(C₁-C₄)-alkyl, or -NH-C(O)-O-(CH₂)-phenyl;

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M is a hydrogen atom or (C₁-C₃)-alkyl-; and

R⁴ and R⁵ are independently of one another hydrogen atom or methyl.

18. (New) A compound of formula I as claimed in claim 14, wherein

R₀ is phenyl, wherein phenyl is mono-, di- or trisubstituted independently of one another by R²;

R² is halogen; (C₁-C₄)-alkyloxy-, wherein alkyloxy is unsubstituted or substituted by halogen or an amino group; or -(C₁-C₄)-alkyl, wherein alkyl is unsubstituted or substituted by an amino group or halogen;

Q and Q' are different and are a direct bond or -O-;

X is -(C₁-C₃)-alkylene-;

D is carbon;

the substructure of formula III is phenyl, wherein phenyl is unsubstituted or mono-, di- or trisubstituted independently of one another by R¹;

R¹ is halogen; -NO₂; -CN; -NH₂; -OH; -SO₂-NH₂; (C₁-C₄)-alkylamino-, (C₁-C₄)-alkyloxy-, (C₁-C₄)-alkyl-, or (C₁-C₄)-alkylsulfonyl-, wherein the alkyl of each group is unsubstituted or mono-, di- or trisubstituted independently of one another by R¹³; -C(O)-NR¹⁴R¹⁵, wherein R¹⁴R¹⁵ independently of one another are hydrogen atom or (C₁-C₂)-alkyl-; R¹¹R¹²N-, wherein R¹¹ and R¹² are as defined above; or -NR⁴R⁵;

R¹³ is halogen, -CF₃, -NH₂, -OH, (C₁-C₄)-alkyl-, or (C₁-C₄)-alkyloxy-;

R₁₀ is a hydrogen atom; and

V is a fragment of the formulae IIa, IIb, IIc or IId as defined above, wherein

L is a direct bond or (C₁-C₂)-alkylene-;

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A is a hydrogen atom, -C(O)-OH, -C(O)-O-(C₁-C₄)-alkyl, -C(O)-NR⁴R⁵, or -(C₁-C₄)-alkyl;

U is -NH₂, methyl, -NH-C(O)-O-(C₁-C₄)-alkyl, or -NH-C(O)-O-(CH₂)-phenyl;

M is a hydrogen atom or methyl; and

R⁴ and R⁵ are independently of one another hydrogen atom or methyl.

19. (New) A compound of formula I as claimed in claim 14, wherein

R₀ is phenyl, wherein phenyl is disubstituted independently of one another by R²;

R² is halogen; (C₁-C₂)-alkyloxy-, wherein alkyloxy is unsubstituted or substituted by an amino group; or-(C₁-C₄)-alkyl, wherein alkyl is unsubstituted or substituted by an amino group;

Q and Q' are different and are a direct bond or -O-;

X is -CH₂-CH₂-;

D is carbon;

the substructure of formula III is phenyl, wherein phenyl is unsubstituted or mono-, di- or trisubstituted independently of one another by R¹;

R¹ is halogen; -OH; -NH₂; -C(O)-NR¹⁴R¹⁵, wherein R¹⁴R¹⁵ independently of one another are hydrogen atom or (C₁-C₂)-alkyl-; or (C₁-C₃)-alkyloxy-, or (C₁-C₃)-alkyl-, wherein the alkyl group of each is unsubstituted or mono-, di- or trisubstituted independently of one another by R¹³;

R¹³ is fluorine or chlorine;

R₁₀ is hydrogen atom; and

V is a fragment of the formulae IIa, IIb, IIc or IId as defined above; wherein

L is a direct bond or (C₁-C₂)-alkylene-;

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A is a hydrogen atom, -C(O)-OH, -C(O)-O-(C₁-C₄)-alkyl, -C(O)-NR⁴R⁵, or -(C₁-C₄)-alkyl;

U is -NH₂, methyl, -NH-C(O)-O-(C₁-C₄)-alkyl, or -NH-C(O)-O-(CH₂)-phenyl;

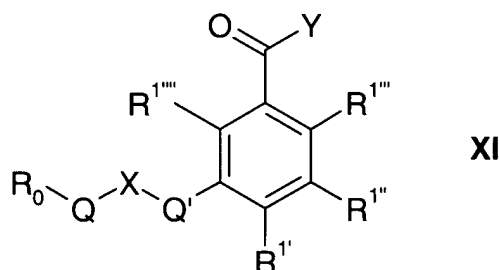
M is a hydrogen atom; and

R⁴ and R⁵ are independently of one another hydrogen atom or methyl.

20. (New) A process for the preparation of a compound of the formula I as claimed in claim 14, comprising

a) linking a building block of formula XI with a fragment of the formula XII,

wherein formula XI is:



wherein:

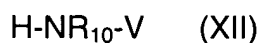
R₀, Q, Q', and X, are as defined in claim 14, and

R^{1'}, R^{1''}, R^{1'''}, R^{1''''}, are a hydrogen atom or R¹ as defined in claim 14,

Y is a nucleophilically substitutable leaving group or a hydroxyl group,

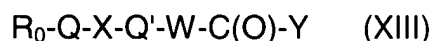
wherein R₀, Q, R^{1'}, Q' or X can also be present in protected form or in the form of precursor groups, and

wherein formula XII is:



wherein R_{10} and V are as defined in claim 14, and can also be present in protected form or in the form of precursor groups, or

b) coupling a fragment of formula XIII with formula XII, wherein formula XIII is:



wherein R_0 , Q, Q', and X are as defined in claim 14,

W is the substructure of formula III, and

Y is a nucleophilically substitutable leaving group or a hydroxyl group,

wherein R_0 , Q, Q', W, or X can also be present in protected form or in the form of precursor groups.

21. (New) The method of claim 10, wherein the thrombosis occurs as a result of at least one of thrombolytic therapy, surgery, a myocardial infarction, angina, or stroke.

22. (New) The method of claim 10, wherein the restenosis occurs as a result of at least one of angioplasty, coronary heart disease, adult respiratory distress syndrome, multi-organ failure, stroke, viral infections, cancer or a disseminated intravascular clotting disorder.

23. (New) The method of claim 20, wherein when R_0 , Q, $R^{1'}$, Q' or X is a hydroxy group, it is attached to a polystyrene resin.

24. (New) A method of treating blood coagulation disorders, inflammation, fibrinolysis, cardiovascular disorders, restenosis, transient ischemic attacks, and thrombosis comprising administering the pharmaceutical preparation of claim 9 to a host in need thereof.

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25. (New) The method of claim 24, wherein the thrombosis occurs as a result of at least one of thrombolytic therapy, surgery, a myocardial infarction, angina, or stroke.

26. (New) The method of claim 24, wherein the restenosis occurs as a result of at least one of angioplasty, coronary heart disease, adult respiratory distress syndrome, multi-organ failure, stroke, viral infections, cancer or a disseminated intravascular clotting disorder.

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